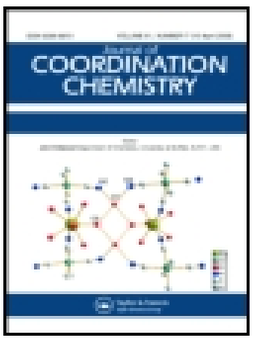

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NITROSUBSTITUTED HYDROXAMATE LIGANDS IN NEW TRIPHENYLTIN(IV) COMPLEXES AS PROSPECTIVE ANTIMICROBIAL AGENTS

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Abstract

New triphenyltin(IV) hydroxamate complexes, [$Ph_3Sn(4\text{-}NO_2CnH)$] (**1**) and [$Ph_3Sn(4\text{-}NO_2BzH)$] (**2**) have been synthesized by the reactions of Ph_3SnCl with potassium 4-nitrocinnamo hydroxamate [$4\text{-}NO_2C_6H_4CHCHCONHOK$] ($KHL^1$) and potassium 4-nitro benzohydroxamate [$4\text{-}NO_2C_6H4CONHOK$] (KHL^2). The complexes were synthesized in 1:1 molar ratio in $MeOH+C_6H_6$ and characterized by physicochemical and IR, ^1H NMR and mass spectrometry. The bidentate hydroxamate involving bonding through carbonyl and hydroxamic oxygen (O, O coordination) has been inferred from IR spectra. The electrochemical behavior of complexes has been analyzed. Quasi-irreversible two electron metal-centered cathodic process of type Sn^{IV}/Sn^{II} redox couple was indicated by cyclic voltammetric technique. The thermal behavior of **1** and **2** studied by TGA have shown continuous decomposition to yield $Sn+0.5SnO_2$ and SnO_2 as final residues. The *in-vitro* antimicrobial activity assays of **1** and **2** against pathogenic gram+ve bacteria (*Bacillus subtilis* and *Staphylococcus aureus)*, gram–ve bacteria (*Salmonella typhi* and *Pseudomonas aeruginosa)*, and fungi (*Aspergillus fumigatus* and *Alternaria alternata*) were doneby MIC method. The complexes have exhibited appreciable antimicrobial activity relative to the respective standard Gentamycin and Nystatin drugs.

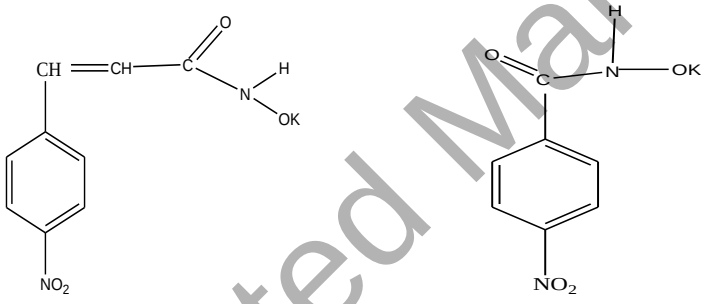
Keywords
Triphenyltin(IV) complexes, 4-Nitrocinnamohydroxamate, 4-Nitrobenzohydroxamate, spectral studies, antimicrobial activity.

1. Introduction

Hydroxamic acids RC(O)NHOH, an important class of organic bioligands and bioactive compounds, have been used as supporting ligands in organometallic chemistry and biology. They have excellent chelating properties on account of tautomerism, displaying hydroxamato/imato binding modes and potential as therapeutic agents (1-4). The medicinal chemistry and pharmacology of hydroxamic acid derivatives and their ability as potent and selective inhibitors of a range of metalloenzymes continue to arouse interest (5). The physiological role of hydroxamic acids as siderophores for the development of bio conjugates utilized as carriers to selectively deliver antimicrobial prodrug to the site of action is well–documented (6). Many reports on diverse applications of hydroxamic acids reveal that they impact coordination chemistry, chemical biology and medical science (7-11).

Since the synthesis of the first- organotin(IV) compound, diethyltindichloride, by Sir Edward Frankland in 1894, there has been attention towards the synthesis of new organotin(IV) compounds with biologically

active ligands (12) displaying structural diversity and exploiting their biomedical applications (13-24). The biochemical activity of organotin compounds is influenced by the number (mono, di, tri) of organic groups (R) linked to tin, organic ligand (L), structure of complex (nuclearity) and coordination number at tin (geometry). A prominent feature of organotin(IV) coordination chemistry is the large number of structurally diverse Sn-O bound compounds derived from a variety of oxygen ligands of which carboxylic acids (24-31) and hydroxamic acids (32-33) are of interest. A variety of organotin polymers used as anticancer and antiviral agents has been synthesized and characterized (34). Among organotin(IV) compounds, compared to several reports on diorganotin(IV) hydroxamates (35-42) there are only a few reports on triorganotin(IV) hydroxamates. Of $[R_3Sn(IV)]^+$ compounds (43-46) the lower homologues (Me, Et) are more toxic upon oral administration than higher homologues and biological activity of organotin compounds follows the order $R_3Sn^+ > R_2Sn^{2+} > RSn^{3+}$. Hence, in the present work the synthesis and characterization of new triphenyltin(IV) complexes bearing biologically significant hydroxamate ligands display promising coordination with potential antimicrobial activities. As the complexes derived from ligands with electron withdrawing groups ($-NO_2$, -Cl) exhibit higher activity than those with an electron releasing group, nitro substituted hydroxamate ligands have been chosen. Cinnamic acids and their derivatives are drug candidates in tuberculosis being used as traditional medicines (47) and benzohydroxamic acid dominates coordination chemistry.



[4-NO_2CnHK](KHL^1) [4-NO_2BzHK](KHL^2)

Structure of hydroxamate ligands

2. Experimental

Reagent-grade solvents were dried and distilled prior to use. All other chemicals were reagent grade. Triphenyltin chloride (Fluka) was used as received. The purity was checked by a sharp melting point (105^{o}C). The potassium p-nitrocinnamohydroxamate and p-nitrobenzohydroxamate were synthesized by reported method (48). Tin was estimated as tin dioxide by treating the complex with conc. H_2SO_4 (2 volumes) and conc. HNO_3 (3 volumes) with heating to 800^{o}C. Elemental analyses were performed on a Carlo-Erba 1106 Elemental analyzer (Elemental Vario EL III). The molar conductance (10^{-3} M solution in methanol) was obtained on an Elico Conductivity Bridge type CM82T at 25±0.1C. The molecular weights of complexes were determined by the Rast Camphor method. IR spectra of complexes were recorded as KBr pellets on a Nicolet-5700 FTIR spectrophotometer. ^{1}H NMR spectra of complexes were recorded on a BRUKER AVANCE II 400 spectrometer using TMS as an internal standard and DMSO (deuterated) as solvent. Electron spray ionization

mass spectra were recorded in ES positive and negative modes (depending on the sign of the applied electrical field) on WATERS, Q-TOF MICROMASS (ESI-MS) mass spectrometer having mass range of 4000amu in quadurpole and 20,000 amu in TOF. In the positive ion mode protonated and/or alkali adduct analyte molecules and in negative ion mode operation peaks corresponding to deprotonated analyte molecules are observed. Cyclic voltammetric experiments were carried out on an Autolab Potentiostat 128N electrochemical analyzer in methanol in a single compartment cell of volume 20-25mL containing a three-electrode system with a Pt-disk working electrode, Pt-wire as auxiliary electrode and Ag/AgCl electrode as a reference electrode. The supporting electrolyte was 0.4 M KCl in milli-Q water. Thermograms (TGA curves) were recorded in N_2 atmosphere on a SDTQ600V20.9 Build20 thermal analyzer from room temperature to 1000^0 C at heating rate of 10^0 C/min.

2.1 Synthesis

2.1.1 [$Ph_3Sn(4\text{-}NO_2CnH)$](I)

To a solution of Ph_3SnCl (2.00 g, 0.001 mol) in benzene (20 ml) was added an equimolar amount of potassium 4-nitrocinnamohydroxamate (1.271g, 0.001 mol) in methanol (20 ml). The reaction mixture was refluxed for 12 h to ensure completion of reaction. The white solid formed during the course of the reaction was filtered off and identified as KCl (1.023g). The excess solvent from the filtrate was removed by distillation and the concentrate was treated with distilled petroleum ether giving a light brown solid which was dried under vacuum. It was recrystallized from 1:1 mixture of methanol and diethylether.

Yield: 3.09g (81%), M.p 115.0 ^{0}C, $C_{27}H_{22}O_4N_2Sn$ (557): Calcd. C 58.16, H 3.94, N 5.02, Sn 21.36; Found C 58.15, H 3.92, N 5.01, Sn 21.35; $\wedge_m$ 0.78Scm^2mol^{-1}. IR 3110(m)(N-H), 3050(w), 2956(m), 1727(s), 1599(s)(C=O), 1509(s), 1428(s), 1330(m)(C-N), 1307(m), 1173(s), 1078(s), 946(s)(N-O), 843(s), 714(s), 689(s), 536(m)(Sn-O). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.75 (s, 1 H, NH), 7.34-7.45 (m, 15 H, ArH), 7.85 (d, *J* = 6.9 Hz, 6 H,C=C and ArH).

2.1.2 [$Ph_3Sn(4\text{-}NO_2BzH)$] (II)

To a solution of Ph_3SnCl (2.01 g, 0.001 mol) in benzene (20 ml) was added an equimolar amount of potassium 4-nitrobenzohydroxamate (0.472g, 0.001 mol) in methanol (20 ml). The reaction mixture was refluxed for 12 h to ensure completion of the reaction during which a white solid was formed. It was filtered off and identified as KCl (0.63g). The excess solvent from the filtrate was removed by distillation and the concentrate was treated with distilled petroleum ether giving light yellow solid. It was dried under vacuum and recrystallized from 1:1 mixture of methanol and diethylether.

Yield: 1.151g (76.6%), m.p 99.0 ^{0}C, $C_{25}H_{20}O_4N_2Sn$ (531) Calcd. C 56.49, H 3.76, N 2.63, Sn 22.41; Found C 56.50, H 3.77, N 2.62, Sn 22.39: $\wedge_m$ 0.72Scm^2mol^{-1}. IR-3125((w)(N-H), 3015(m), 1727(s), 1599(m)(C=O), 1510(m), 1535(s), 1330(s)(C-N), 1070(s), 996(s)(NO), 843(s), 714(s), 689(s), 550(m), 500(s)(Sn-O). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.91 (s, 1 H, NH), 7.33–7.45 (m, 9 H, ArH), 7.80 (d, *J* = 6.9 Hz, 1 H, ArH), 7.86 (d, *J* = 6.9 Hz, 3 H, ArH), 8.07– 8.34 (m, 6 H, ArH).

2.2 Antimicrobial activity test

Potassium 4-nitrocinnamohydroxamate and potassium 4-nitrobenzohydroxamate and their triphenyltin(IV) derivatives were screened *in-vitro* for their antibacterial activities on selected Gram-positive bacteria (*Staphylococcus aureus, Bacillus subtilis), and* Gram-negative bacteria *(Salmonella typhi and Pseudomonas aeruginosa)* and antifungal activity against (*Aspergillus fumigatus* and *Alternaria alternata*) fungal isolates. The antimicrobial properties were tested at different concentrations in 10% DMSO employing the standard

Minimum Inhibitory Concentration (MIC) method by two-fold serial dilution using oxidation-reduction colorimetric indicator Resazurin dye. The dye was blue in its oxidized state turning pink in case of antibacterial studies whereas colorless for antifungal studies (Resazurin Microtiter Assay plate (REMA) testing as recommended by National Committee for Clinical Laboratory Standards (NCCLS). MIC is the lowest concentration of the antimicrobial agents that prevents the color change of dye. The commercial antibiotics Gentamycin and Nystatin were used as standard antibacterial and antifungal drugs, respectively, as positive controls for comparison of results. All the samples were tested in triplicate.

2.2.1 MIC determination by two-fold serial dilution

The MIC assay was performed in a 96-well micro-titre plate. The stock solution 500 μg/mL was prepared in 10% DMSO which was used for further dilutions. 100 μL of Muller-Hinton broth was added into all the wells of a sterile 96-well microtiter plate. 100 μL of complex solution were placed in the first well of each column except in column with +ve control (100 μL broth + 10 μL microorganism + 10 μL antibacterial/antifungal drug) and –ve control (100 μL broth + 10 μL microorganism). After proper mixing (broth + test complex) 100 μL was withdrawn from the first well with a sterile tip and the same was added to 100 μL of broth in the 2^{nd} well. Then 100 μL solution was withdrawn from the 2^{nd} well and added to the 3^{rd} well. In this way a range of two-fold serial dilutions were prepared starting with 500 μg/mL and diluted to 250, 125, 62.50, 31.25, 15.62, 7.81 and 3.91 μg/mL followed by addition of 10 μL of resazurin dye indicator (0.18% in distilled water). The plates are incubated at 37^{o}C and the growth of bacteria/ fungi were recorded after 12/72 h. The lowest concentration of test complex that inhibited the growth of microorganisms were recorded as MIC. Gentamycin and Nystatin were used as standard antibacterial and antifungal drugs. To evaluate the role of solvent in biological screening, if any, separate studies were carried out with 10% DMSO. The solvent did not show any activity. All the experiments were carried out in triplicate.

2.3 Statistical Analysis

Statistical analysis was performed using standard t-test and p values of less than 0.05 were considered significant. The data are represented as ±SD.

3. Results and discussion

The reactions of Ph_3SnCl with 4-NO_2CnHK (KHL^1) and 4-NO_2BzHK (KHL^2) in predetermined 1:1 molar ratio (metal:ligand) in methanol + benzene under reflux afforded the formation of complexes [Ph_3Sn(4-NO_2CnH)] and [Ph_3Sn(4-NO_2BzH)] in quantitative yields according to the Scheme1.

The stoichiometric composition of isolated complexes has been established by elemental analyses (tin, carbon, hydrogen and nitrogen). Complexes are light brown and light yellow solids. The molar conductance values of 10^{-3}M solutions in methanol (0.78 and 0.72 Scm^2mol^{-1}) are too low to be attributed to 1:1 electrolyte hence indicate non-electrolytes (49). The molecular weight determination of complexes by Rast's camphor method has indicated these to exist as monomers in the solid state.

3.1 IR Spectra

The formation of complexes has been confirmed from a comparison of their IR spectra with those of the free ligands recorded in 4000-250 cm^{-1}. IR spectra of free (4-NO_2CnHK) and (4-NO_2BzHK) exhibited diagnostic bands due to νNH mode at 3108 and 3230 cm^{-1}; νCN at 1341 and 1382 cm^{-1}, νC=O at 1638 and 1620 cm^{-1} and νN-O at 920 and 935 cm^{-1}, respectively. Ph_3Sn[4-NO_2CnH] and Ph_3Sn[4-NO_2BzH] displayed bands due to ν(N-H) at 3110 and 3111cm^{-1}, ν(C=O) at 1593 cm^{-1}; ν(C-N) at 1333, 1334 cm^{-1} and ν(N-O) at 984 and 994 cm^{-1}, respectively [Fig.S1]. The shift in ν(C=O) to lower wavenumber by 45 and 27 cm^{-1}, respectively, relative to respective free ligands indicated that the chelate ring formed weakens the carbonyl bond

diminishing carbonyl double bond character and increasing the N-O bond strength [Fig.S2]. The shifts in νN-H and νC-N occurred due to electron redistribution resulting from resonance within the chelate ring whereby the C-N bond may have more partial double bond character. The observed shifts are suggestive of bonding through carbonyl and hydroxamic oxygens (O,O coordination) and non-participation of nitrogen in bonding. The bands at 536 and 500 cm^{-1} in **1** and **2** have been assigned to νSn-O (50-53).

3.2 ^{1}H NMR Spectra

A comparison of ^{1}H NMR spectra of complexes with those of free ligands has further substantiated their formation. The free 4-NO_2CnHK exhibited signals due to NH, aromatic ring protons and aliphatic protons (CH=CH) at δ 8.0 (s, 1H), 7.18-7.69 (m, 4H) and 5.0-6.5 (m, 2H), respectively. The ^{1}H NMR spectrum of Ph_3Sn[4-NO_2CnH] in DMSO-d_6 displayed signals at δ 3.75 (s, 1 H, NH), 7.34-7.45 (m, 15 H, ArH), 7.85 (d, *J* = 6.9 Hz, 6 H, CH=CH and ArH), respectively. The free 4-NO_2BzHK exhibited signals due to NH and aromatic ring protons at δ 8.0 and 7.21-7.68, respectively, while ^{1}H NMR spectrum [Ph_3Sn(4-NO_2BzH)] displayed these at δ 3.91 (s, 1 H, NH), 7.33–7.45 (m, 9 H, ArH), 7.80 (d, *J* = 6.9 Hz, 1 H, ArH), 7.86 (d, *J* = 6.9 Hz, 3 H, ArH), 8.07– 8.34 (m, 6 H, ArH) [Fig S3, Fig S4)]. The observed downfield shifts in aromatic ring proton resonances compared to free ligands may be ascribed to deshielding of protons upon complexation.

3.3 Mass Spectra

Although mass spectrometry is the most accurate microanalytical technique to assign structures of various molecules, only a few scattered reports describe mass spectra of organotin compounds, perhaps on account of the poly-isotopic nature of tin resulting in relatively complex but highly distinctive isotope patterns or overlapped patterns and also that these undergo large fragmentation because of their low bond dissociation energies under electron impact at inlet temperature (54-57). The natural abundance of ten characteristic natural tin isotopes ^{112}Sn, ^{114}Sn, ^{115}Sn, ^{116}Sn, ^{117}Sn, ^{118}Sn, ^{119}Sn, ^{120}Sn, ^{122}Sn and ^{124}Sn are 0.97, 0.66, 0.34, 14.54, 7.68, 24.22, 8.59, 32.58, 4.63 and 5.79, respectively by which the presence or absence of a tin isotope in individual ions can be validated (58). The positive and negative-ion mode mass spectra of [Ph_3Sn(4-NO_2CnH)] [Figs.1a,b] did not display the molecular ion peak. In positive-ion mode spectra the base peak at m/z(%) 351(100) corresponded to $[Ph_3Sn]^+$ and a fragment ion at m/z(%) 383(4.64) to $[Ph_3SnNHO+2H]^+$. In negative-ion mode the base peak at m/z(%) 205(100) corresponding to$[HL^1-2H]$ and other fragment ions at (m/z)(%) 352(7.6), 234(61.18), 230(8.17), 192(4.93), 148(4.3) and 131(6.86) corresponded to $[Ph_3Sn+H]$, $[Ph_3+3H]^-$, $[HL^1+CO-3H]^-$, $[HL^1-O]^-$, $[HL^1-CONHO]^-$ and $[HL^1-CONHO-O]^-$, respectively. The mass spectral data and fragmentation patterns are given in (Tables 1 and 2) [Schemes 1S and Scheme 2S]. The isotopic pattern of [Ph_3Sn(4-NO_2CnH)] is given in (Table 3)[Fig. 1c]

The positive ion-mode spectrum of **2** exhibited both di- and monotin fragments. The ditin fragments observed at m/z (%) 717(4.24) and 639(5.80) corresponded to $[Ph_3SnOSnPh_3]^+$ and $[Ph_3SnOSnPh_2]^+$, respectively. The base peak at m/z(%) 351(100) corresponded to $[Ph_3Sn]^+$. The other fragment ions at m/z(%) 253(5.21) and 221(6.78) accounted for $[SnC_6H_4CONHO]^+$ and $[SnC_6H_4CO]^+$ respectively.

The ESI negative-ion spectrum of [Ph_3Sn(4-NO_2BzH)](II) [Figs.2a,b] displayed the molecular ion peak at m/z (%) 531(11.44) as well as fragment ions of higher molecular mass than that of the mononuclear complex. The base peak at m/z(%) 557(100) corresponded to $[M+CO-3H]^-$. The ditin fragment ion at m/z(%) 1009(11.22) corresponded to $[2M-CONHO+5H]^-$. The other fragment ions at m/z(%) 620(23.32), 230(3.42), 205(11.95), 181(55.53), 166(82.94), 122(21.28), 92(4.59) and 58(7.94) corresponded to $[M+PhO-5H]^-$$[PhSnO+OH]^-$, $[HL^2+CO-4H]^-$, $[HL^2]^-$, $[HL^2-O+2H]^-$, $[HL^2-CONHO]^-$, $[HL^2-CONHO-2O]^-$ and

[CONO]$^{-}$, respectively (Tables 4 and 5), [Scheme 3S, Scheme 4S]. The isotropic pattern of the complex [$Ph_3Sn(4\text{-}NO_2BzH)$] are given in (Table 6) [Fig. 2].

Based upon physicochemical and spectral studies, distorted trigonal bipyramidal geometry of complexes have tentatively been proposed and structure of complexes has designed by using chemcraft [Figs.3 and 4].

3.4 Cyclic Voltammetry

The ligands ($4\text{-}NO_2CnHK$) and ($4\text{-}NO_2BzHK$) displayed reductive and oxidative peaks at -0.913, +0.867V and +0.857, -0.881V, respectively. [$Ph_3Sn(4\text{-}NO_2CnH)$] exhibited two reductive peaks at -0.550 and +0.652V and one anodic peak at -0.593V as a counterpart of former cathodic peak (Table 7) [Figs.5 a,b]. The [$Ph_3Sn(4\text{-}NO_2BzH)$] showed two cathodic peaks at -0.498 and +0.731V and one anodic peak at -0.574V [Figs.6 a,b]. The electrochemical data of ligands and complexes indicated that the electrode process is quasi-reversible. The tin (IV) state is stable to oxidation but easily reduced to tin (II) by two electron reduction in agreement with redox active behaviour and theoretical interpretation of cytotoxic diorganotin(IV) cycloalkylhydroxamate complexes with different sizes exhibiting an irreversible two electron cathodic process of type Sn^{IV} / Sn^{II} in methanol solution (59,60).

3.5 Thermal Studies

The thermal behavior of **1** and **2** studied in N_2 shows thermal stability to 115.32 and 98.42 ^{o}C, respectively, after which these undergo continuous decomposition yielding $Sn+0.5SnO_2$ and SnO_2 as residues [Figs.S5a,b].

$$Ph_3Sn[4\text{-}NO_2CnH] \xrightarrow{-65.01\%} Sn + 0.5\ SnO_2$$

$$Ph_3Sn[4\text{-}NO_2BzH] \xrightarrow{-71.46\%} SnO_2$$

3.6 Antimicrobial Activity Studies

3.6.1 Antibacterial activity

The antibacterial activities of free $4\text{-}NO_2CnHK$ (KHL^1), $4\text{-}NO_2BzHK$ (KHL^2), **1** and **2**, have been evaluated against two gram+ve (*Bacillus subtilis*, *Staphylococcus aureus*) and two gram–ve bacteria (*Salmonella typhi and Pseudomonas aeruginosa*). Gentamycin has been used as the standard drug for comparison. KHL^1 and KHL^2 inhibited these bacteria in 62.5-125 µg/mL and 15.62-125 µg/mL range, respectively indicating KHL^2 to be a better antibacterial agent. Complex **2** has significant inhibitory effect against *Salmonella typhi* and *Bacillus subtilis* at MIC 7.81 µg/mL better than **1** at MIC 31.25 and 15.62µg/mL, respectively. The ligands and complexes have moderate activity against *Staphylococcus aureus* at MIC 62.5-125 µg/mL (Table 8) [Fig. 7].

3.6.2 Antifungal activity

The antifungal activities of ligands and complexes have been studied against *Aspergillus fumigatus* and *Alternaria alternata*. KHL^1 and KHL^2 inhibited these fungi at MIC 15.62-62.5 µg/mL and 31.5-15.62 µg/mL, respectively. Complex **1** has enhanced inhibitory effect against test fungi at 7.81 and 31.25µg/mL,

respectively. Complex **2** has good inhibitory effect against *A.alternata* at MIC 7.81 µg/mL. The standard Nystatin drug inhibited these fungi at MIC 3.90 µg/mL and 1.95 µg/mL, respectively (Table 9) [Fig. 8].

There are a few scattered reports of antimicrobial activity of organotin(IV) hydroxamates compared to those derived from other ligands (61-64, 53). The activities of triorganotin(IV) hydroxamates (65) are less studied than diorganotin(IV) hydroxamates (66). Different methodologies and pathogenic bacterial and fungal strains have been assayed in various studies (67). Hence, these factors limit comparison of the antimicrobial assay of triphenyltin(IV) hydroxamates studied herein with those reported earlier.

Comparison of the antimicrobial activities of the ligands and their triphenyltin(IV) derivatives with standard drugs show that the newly synthesized complexes have appreciable inhibitory activity against the studied bacterial and fungal strains finding potential as antimicrobial compounds. The observed antimicrobial activity of **1** and **2** can be ascribed to their efficient diffusion into microbe cells (68, 69) inhibiting the activity of essential enzymes for bacterial growth and interaction with deoxyribose nucleic acid (DNA).

4. Conclusions

The triphenyltin(IV) hydroxamate complexes [$Ph_3Sn(4\text{-}NO_2CnH)$] (**1**) and [$Ph_3Sn(4\text{-}NO_2BzH)$] (**2**) derived from potassium 4-nitrocinnamohydroxamate and 4-nitrobenzohydroxamate ligands have been synthesized in good yields and characterized by physicochemical and IR, ^{1}HNMR and mass spectral techniques. The hydroxamate ligands are bidentate (O, O through carboxyl and hydroxamic oxygens). The complexes are electrochemically active undergoing quasi-irreversible two electron reductions leading to tin in +2 oxidation state. Thermal behavior of **1** and **2** by thermogravimetric technique show these to undergo continuous decomposition to yield $Sn+0.5SnO_2$ and SnO_2, respectively as residues. The *in-vitro* antibacterial assay of ligands **1** and **2** has shown that **2** has pronounced inhibitory effect against *Bacillus subtilis* and *Salmonella typhi* as compared to **1**. The *in-vitro* antifungal activity of ligands and complexes evaluated against *Aspergillus fumigatus* and *Alternaria alternata* show that **1** exhibits good inhibitory effect against *Aspergillus fumigatus* while **2** against *Alternaria alternata*. The results reveal these new complexes as promising antimicrobial agents to be explored for medicinal applications.

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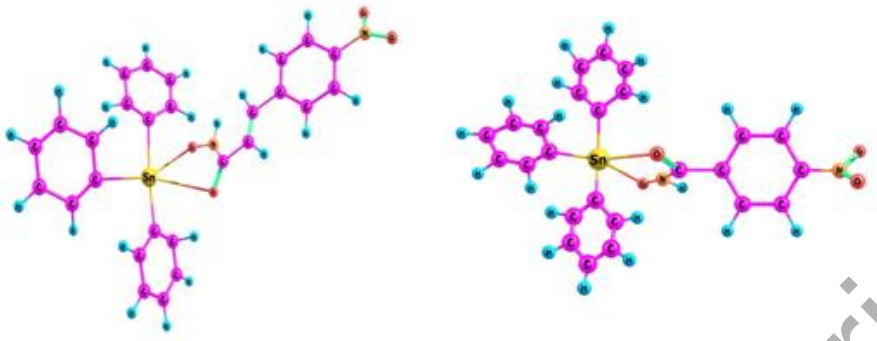
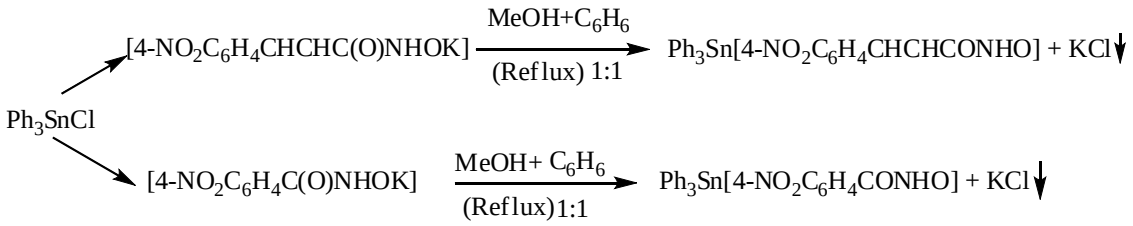
Graphical Abstract





Scheme1. Synthesis of complexes

Figure Captions

Fig 1. (a, b) Mass spectra of Ph_3Sn [4-NO_2C_nH] in (a) ES positive and (b) ES negative mode, respectively

Fig. 1(c) Isotropic pattern of Ph_3Sn[4-NO_2CnH]

Fig. 2 (a, b) Mass spectra of Ph_3Sn [4-NO_2BzH] in (a) ES positive and (b) ES negative mode, respectively

Fig. 2(c) Isotropic pattern of Ph_3Sn[4-NO_2BzH]

Fig. 3 Chemcraft structure of Ph_3Sn [4-NO_2CnH]

Fig. 4 Chemcraft structure of Ph_3Sn [4-NO_2BzH]

Fig. 5 CV of (a) [4-NO_2CnHK] and (b) Ph_3Sn [4-NO_2CnH**]**

Fig. 6 CV of (a) [4-NO_2BzHK] and (b) Ph_3Sn [4-NO_2BzH**]**

Fig. 7 *In vitro* antibacterial activity studies of [$KHL^{1,2}$], (I) and (II) compared to gentamycin

Fig. 8 *In vitro* antifungal activity studies of [$KHL^{1,2}$], (I) and (II) compared to nystatin

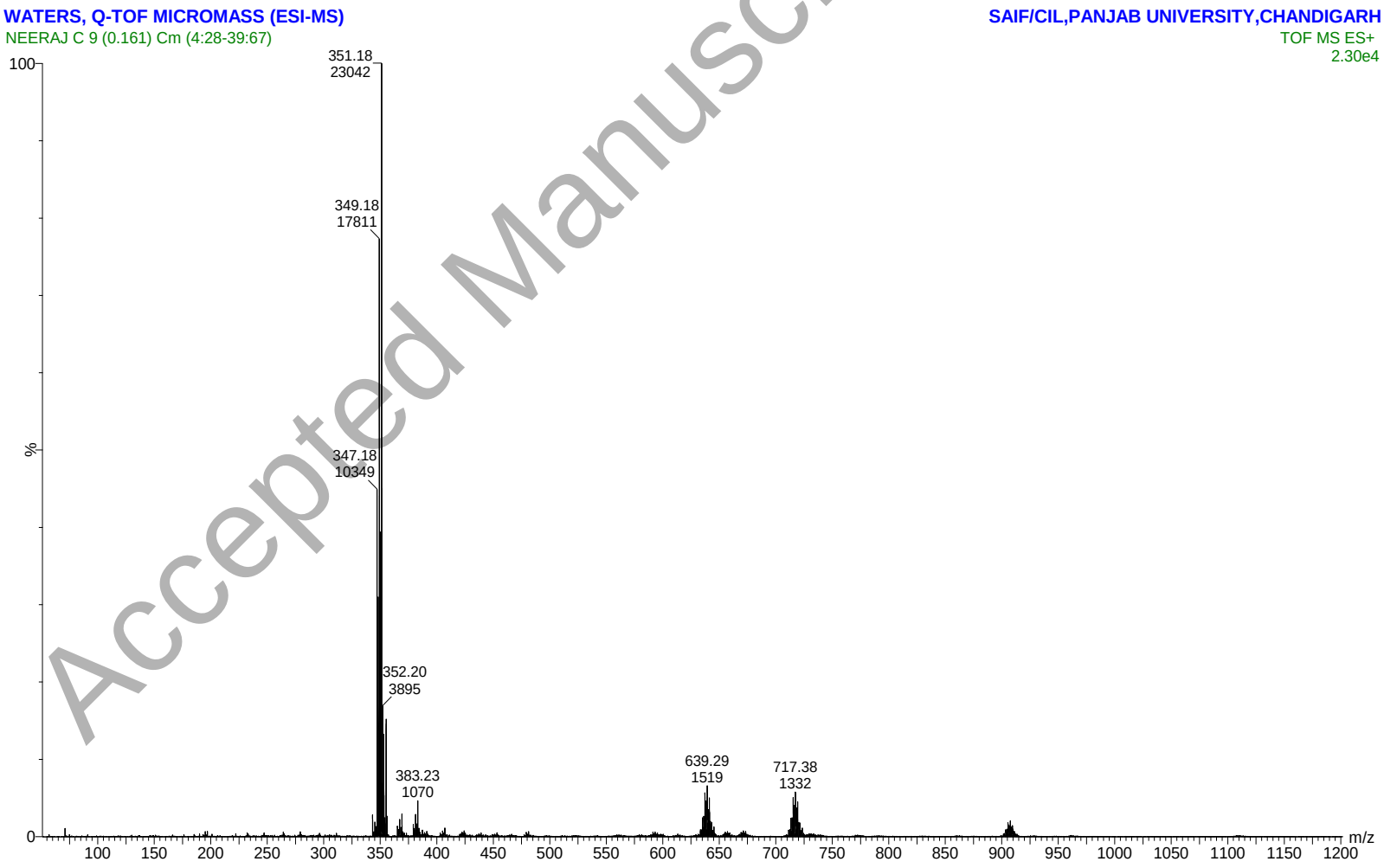
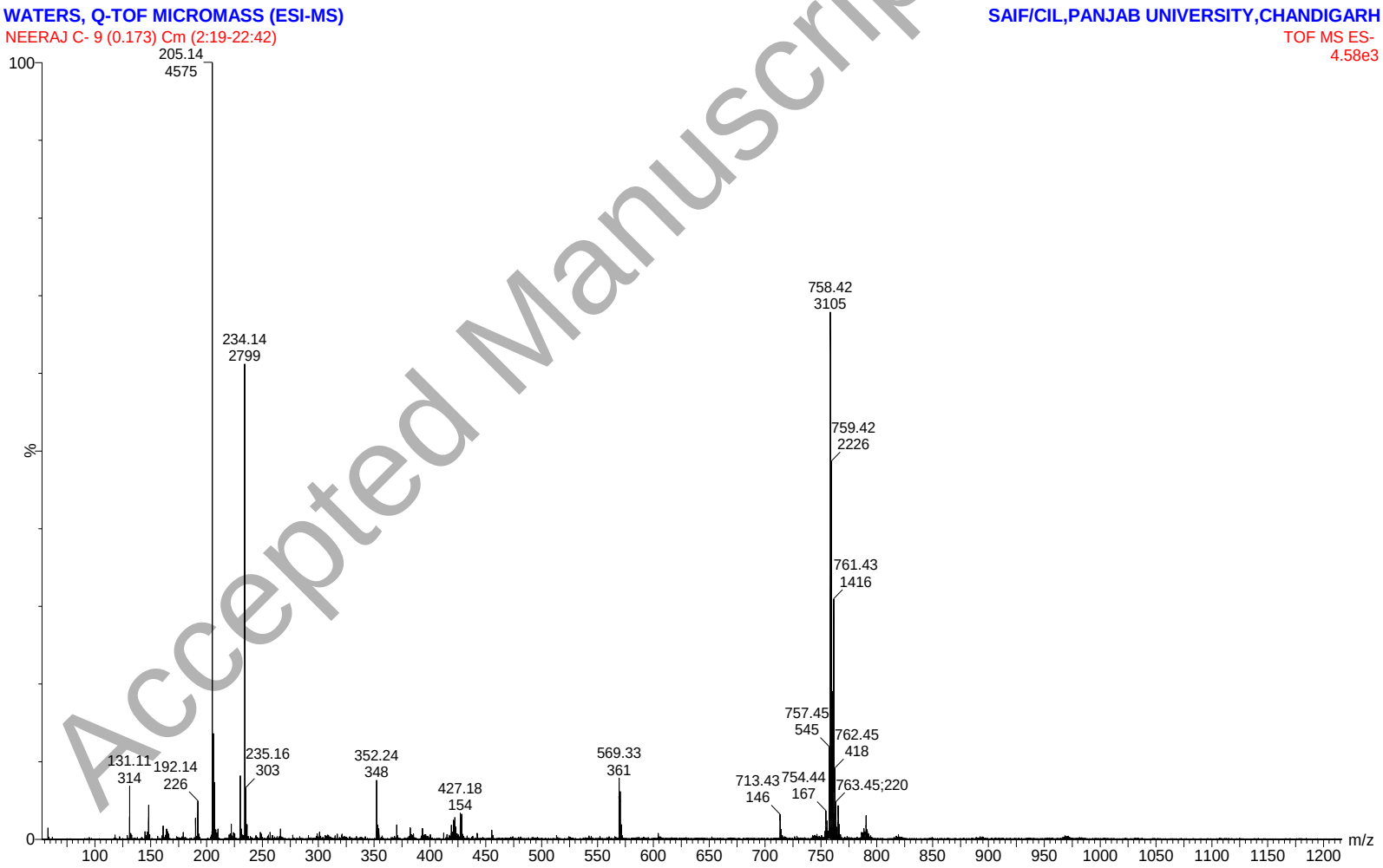


Fig.1(a)



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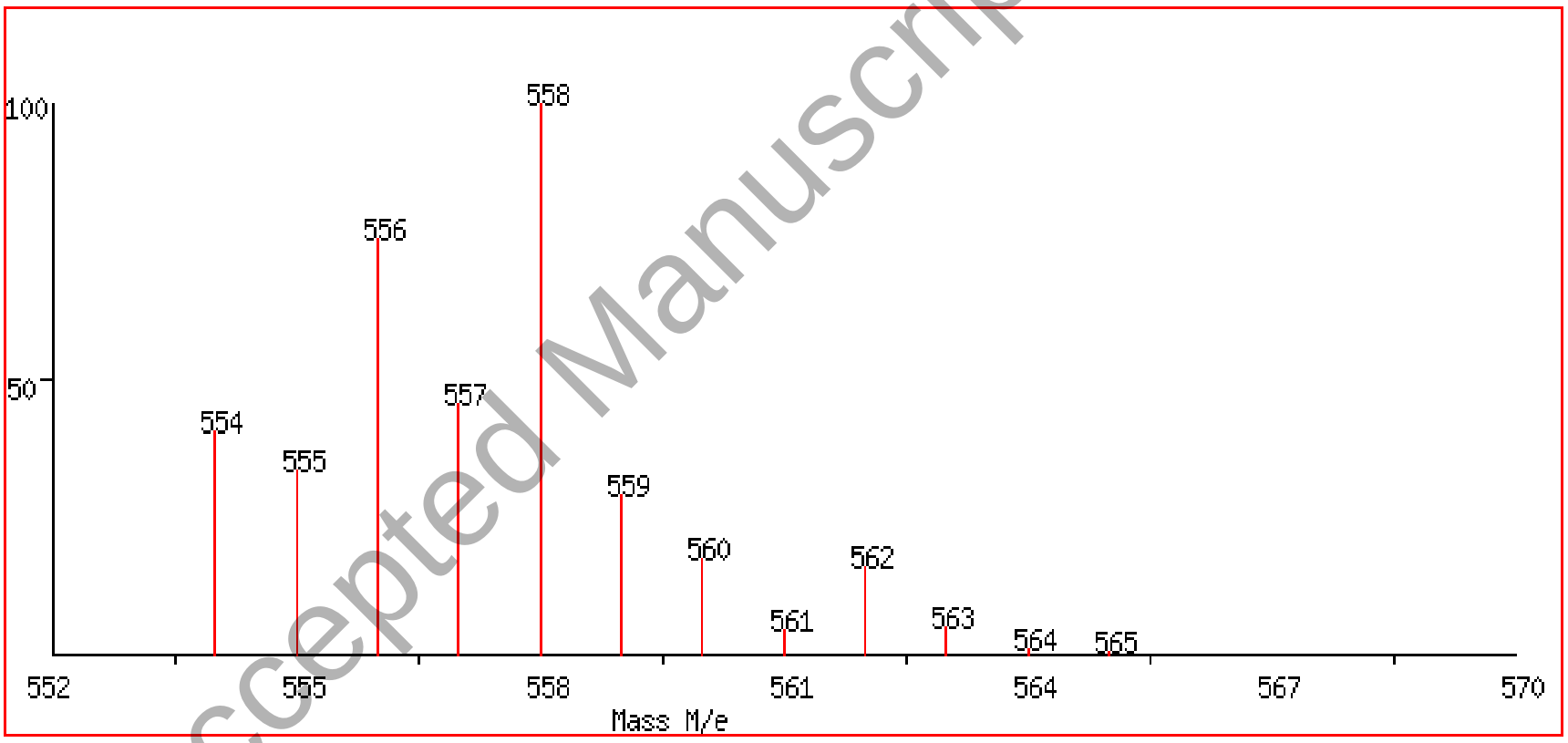


Fig.1(c)

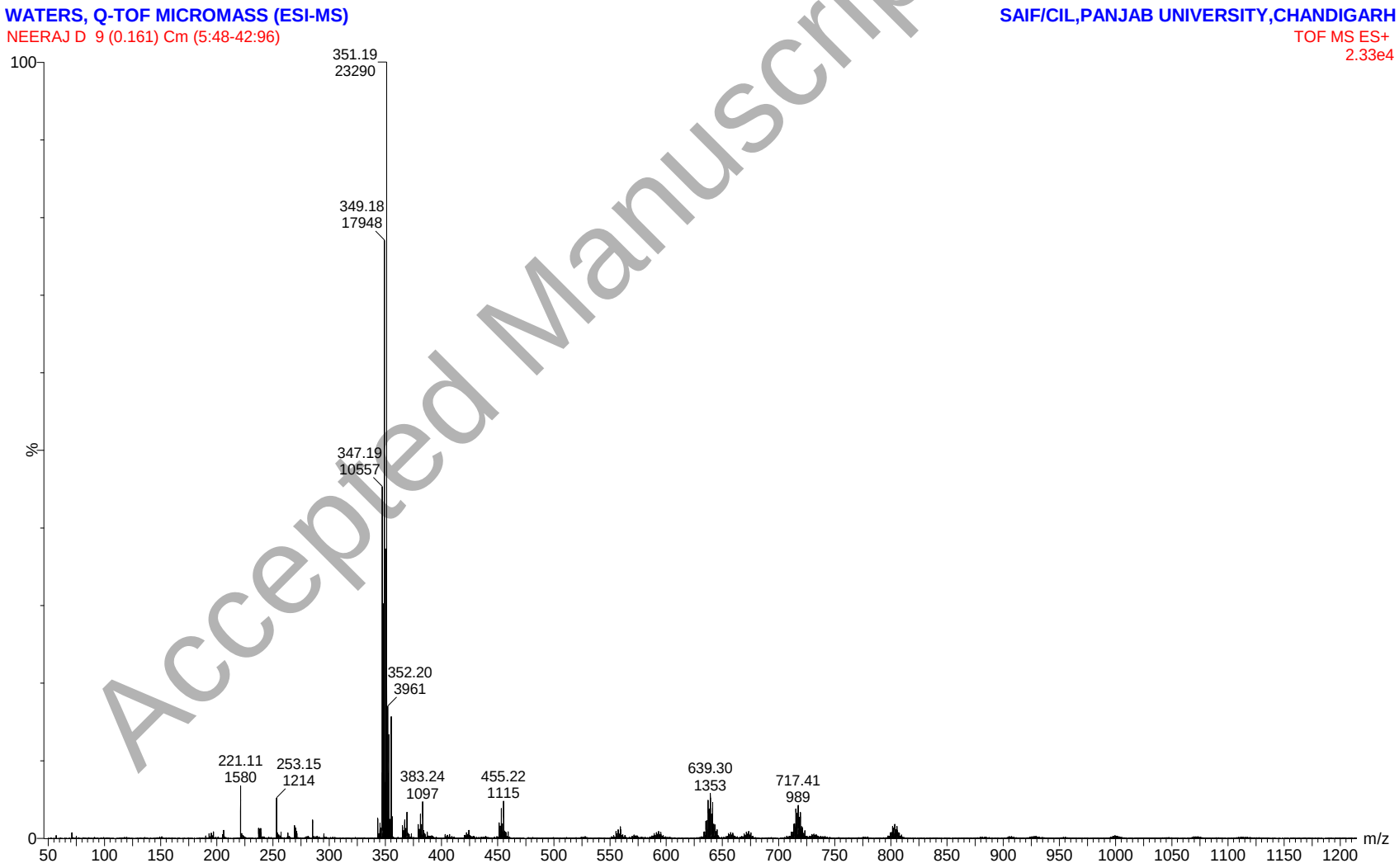
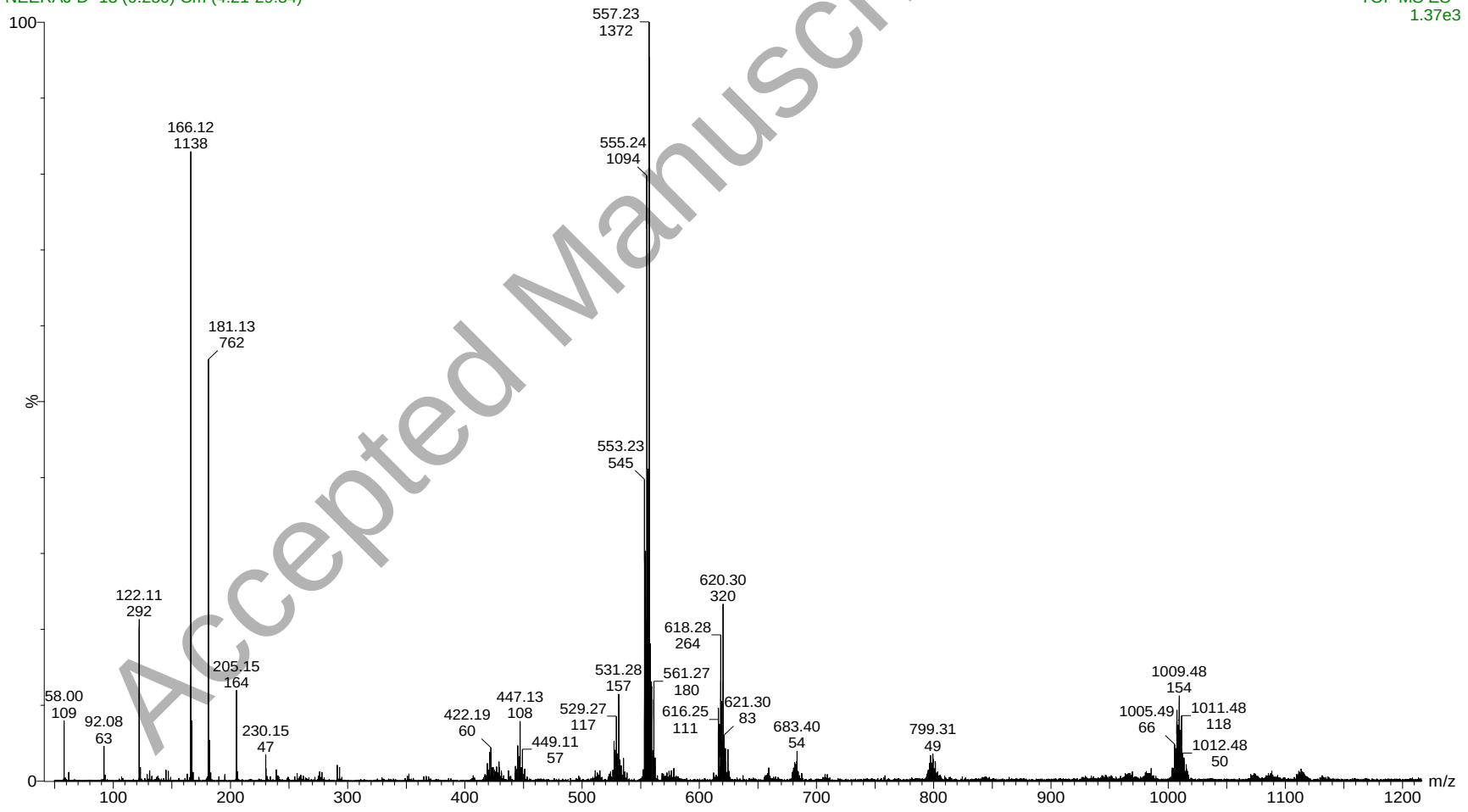


Fig.2(a)



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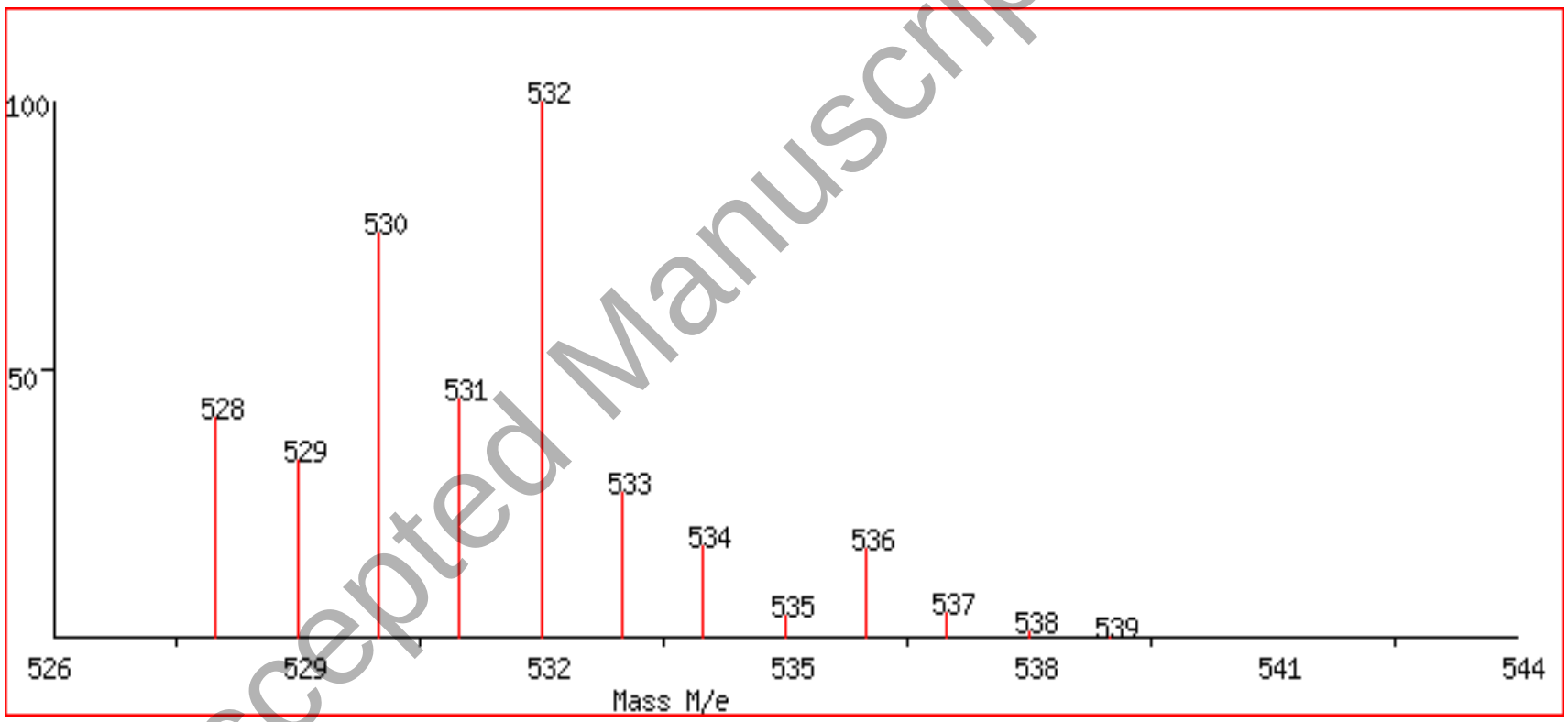


Fig.2(c)

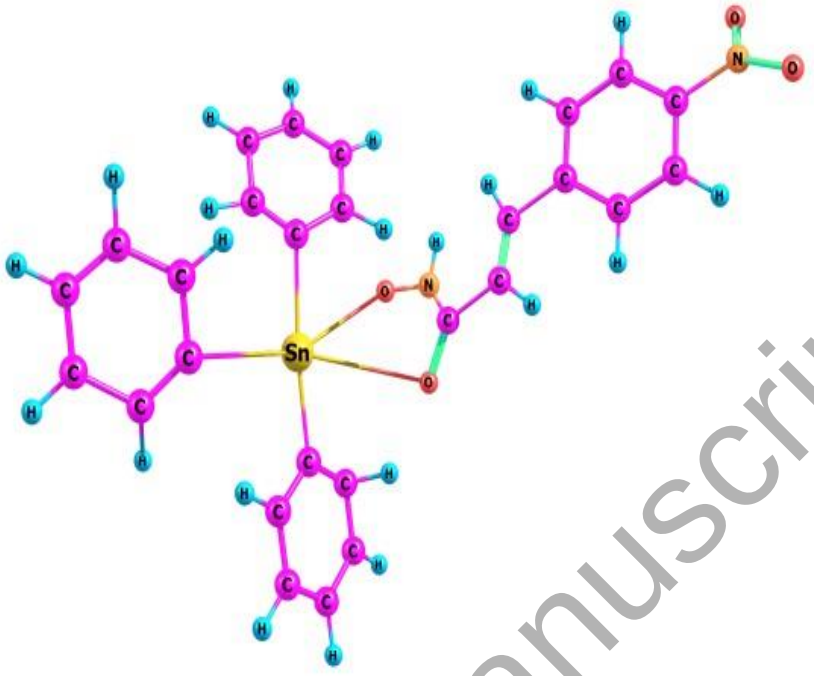


Fig.3

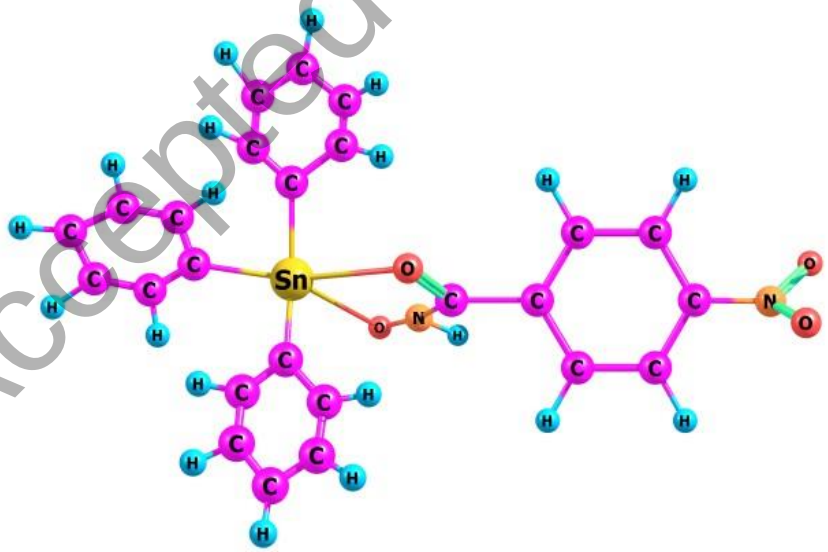
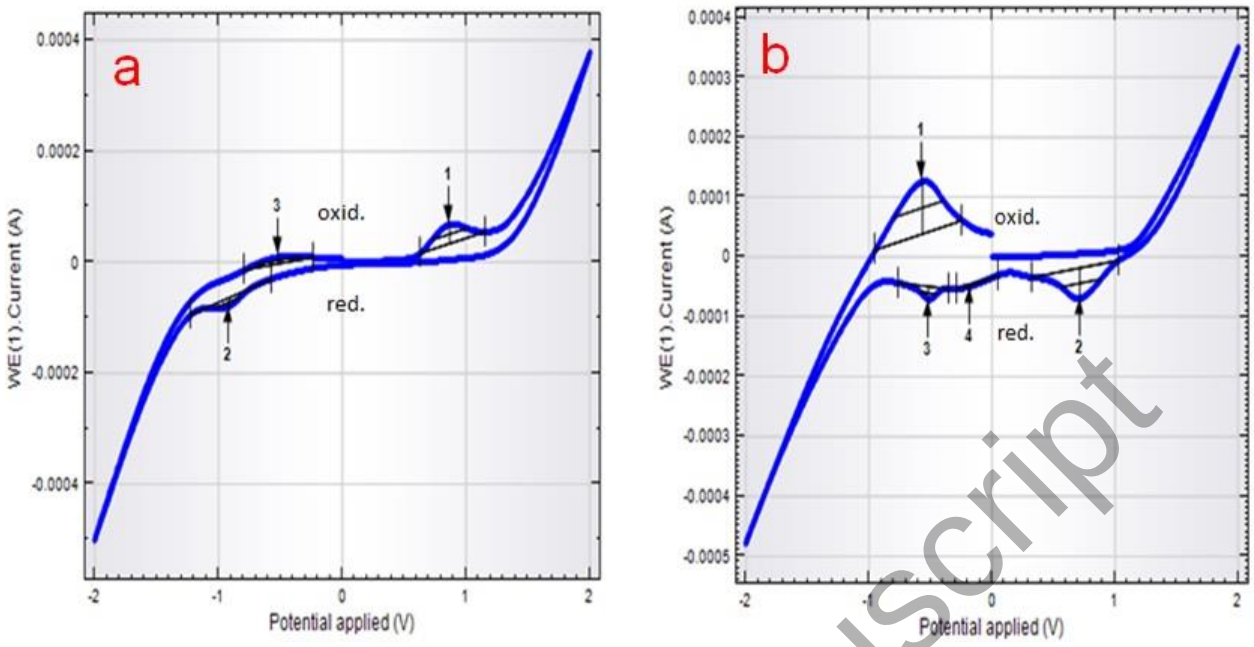
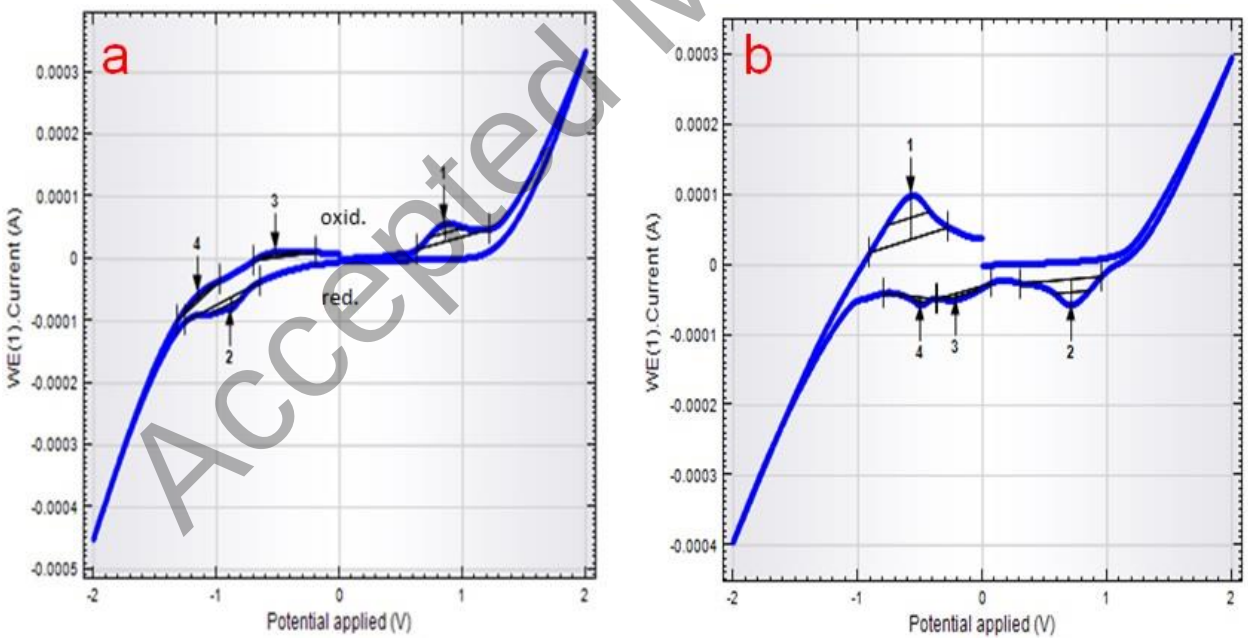


Fig.4



Figs.5(a,b)



Figs.6(a,b)

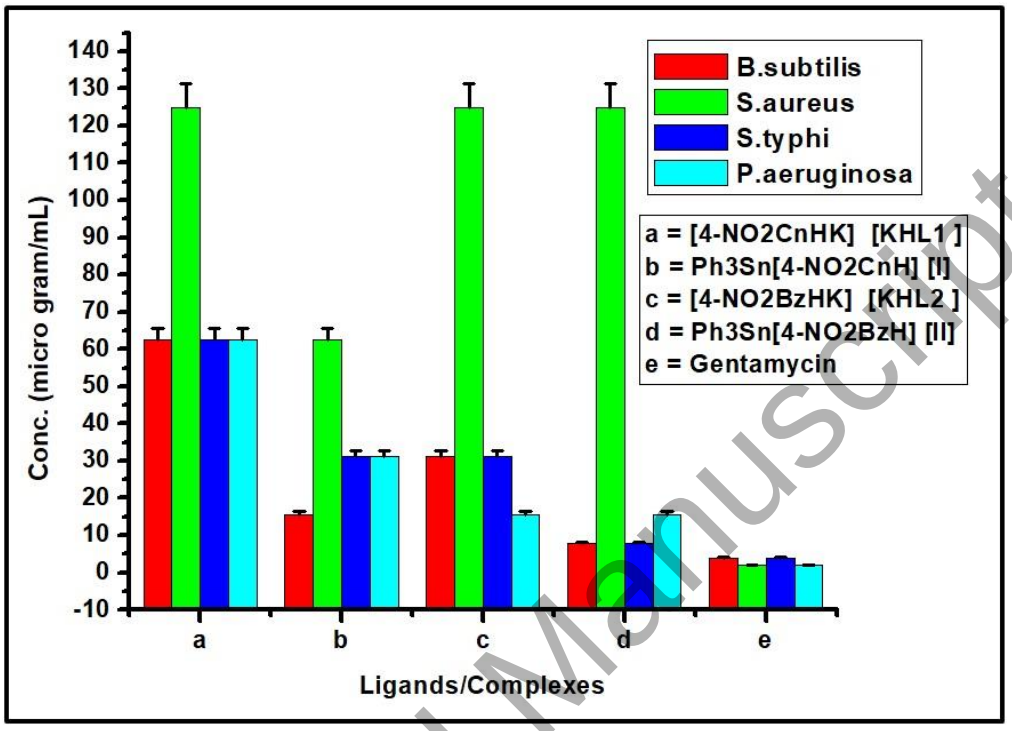


Fig.7

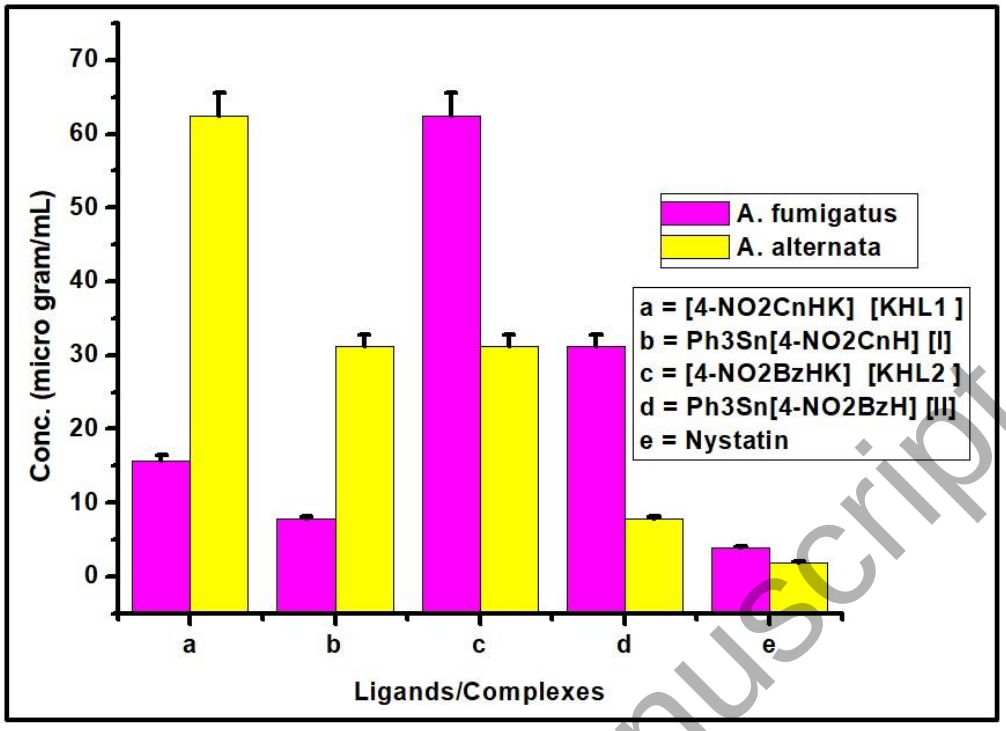


Fig.8

Tables:-

Table 1. Mass Spectral data of $Ph_3Sn[4\text{-}NO_2CnH]$ in ES positive mode

$Ph_3Sn[4\text{-}NO_2C_nH]$ /$Ph_3Sn(HL^1)$ (M)	**m/z(%)**
Monotin fragments $[Ph_3SnNHO+2H]^+$	383(4.64)
$[Ph_3Sn]^+$ (B.P)	351(100)

Table 2 Mass Spectral data of $Ph_3Sn[4\text{-}NO_2CnH]$ in ES negative mode

$Ph_3Sn[4\text{-}NO_2C_nH]$ /$Ph_3Sn(HL^1)$ (M)	m/z(%)
$[Ph_3Sn+H]^-$	352(7.6)
$[Ph_3+3H]^-$	234(61.18)
$[HL^1+CO-3H]^-$	230(8.17)
$[HL^1-2H]^-$ (B.P)	205(100)
$[HL^1-O]^-$	192(4.93)
$[HL^1-CONHO]^-$	148(4.3)
$[HL^1-CONHO-(O)]^-$	131(6.86)

Table 3 Isotropic pattern of $Ph_3Sn[4\text{-}NO_2CnH]$

Mass(m/z)	Intensity(%)	Mass(m/z)	Intensity(%)
554	40.5	560	17.5
555	33.5	561	4.3
556	75.4	562	16
557	45.4	563	4.7
558	100	564	0.8
559	28.8	565	0.1

Table 4 Mass Spectral data of $Ph_3Sn[4\text{-}NO_2BzH]$ in ES positive mode

$Ph_3Sn[4\text{-}NO_2BzH]$ /$Ph_3Sn(HL^2)$ (M)	**m/z(%)**
Ditin fragments $[Ph_3SnOSnPh_3]^+$	717(4.24)
$[Ph_3SnOSnPh_2]^+$	639(5.80)
Monotin frgments $[Ph_3Sn]^+$ (B.P)	351(100)
$[SnC_6H_4CONHO+H]^+$	253(5.21)
$[SnC_6H_4CO+2H]^+$	221(6.78)

Table 5 Mass spectral data of $Ph_3Sn[4\text{-}NO_2BzH]$ in ES negative mode

$Ph_3Sn[4\text{-}NO_2BzH]$ /$Ph_3Sn(HL^2)$ (M)	**m/z(%)**
$[2M\text{-}CONHO+5H]^-$	1009(11.22)
$[M+PhO-5H]^-$	620(23.32)
$[M+CO-3H]^-$	557(100)BP
$[M-H]^-$	531(11.44)
$[PhSnO+OH]^-$	230(3.42)
$[HL^2+CO-4H]^-$	205(11.95)
$[HL^2]^-$	181(55.53)
$[HL^2\text{-}O+2H]^-$	166(82.94)
$[HL^2\text{-}CONHO]^-$	122(21.28)
$[HL^2\text{-}CONHO\text{-}2O]^-$	92(4.59)
$[CONO]^-$	58(7.94)

Table 6 Isotropic pattern of $Ph_3Sn[4\text{-}NO_2BzH]$

Mass(m/z)	Intensity(%)	Mass(m/z)	Intensity(%)
528	40.9	534	17
529	32.9	535	4
530	75.4	536	16.1
531	44.1	537	4.4
532	100	538	0.7
533	26.9	539	0

Table 7. Cyclic voltammetric data of ligands and triphenyltin(IV) hydroxamate complexes

Ligand/Complex	Redox Couple	Epa(V)	Epc(V)	ΔE(mV) (Epa-Epc)	Ipa (A)	Ipc(A)	Ipa/Ipc	$E_{1/2}$(mV)
[4-NO_2CnHK]	-----	+0.866	-0.913	1778	0.00006	-0.0001	0.6	889
Ph_3Sn[4-NO_2CnH]	Sn^{4+}/Sn^{2+}	-0.593	-0.550 +0.652	1245 -----	-0.00013 -----	0.00009 -----	1.44 -----	622.5 -----
[4-NO_2BzHK]	-----	+0.857	-0.881	993	0.00006	-0.0001	0.6	496.5
Ph_3Sn[4-NO_2BzH]	Sn^{4+}/Sn^{2+}	-0.573	-0.498 +0.713	1286 -----	0.0001 -----	-0.00007 -----	1.43 -----	643 -----

Table 8. Antibacterial activity of ligands and complexes by MIC method (µg/mL)

Ligand/Complex	***B. subtilis***	***S.aureus***	***S.typhi***	***P.aeruginosa***
[4-NO_2C_nHK] [KHL^1]	62.5±0.1	125±0.5	62.5±0.5	62.5±0.08
Ph_3Sn[4-NO_2CnH] [I]	15.62±0.1	62.5±0.2	31.25±0.35	31.25±0.45
[4-NO_2BzHK] [KHL^2]	31.25±0.1	125±0.5	31.25±0.4	15.62±0.5
Ph_3Sn[4-NO_2BzH] [II]	7.81±0.05	125±0.5	7.81±0.05	15.62±0.1
Gentamycin	3.90±0.05	1.95±0.1	3.90±0.01	1.95±0.05

Table 9. Antifungal activity of ligands and complexes by MIC method(µg/mL)

Ligand/Complex	***A. fumigatus***	***A. alternate***
[4-NO_2CnHK] [KHL^1]	15.62±0.1	62.5±0.5
Ph_3Sn[4-NO_2CnH] [I]	7.81±0.05	31.25±0.01
[4-NO_2BzHK] [KHL^2]	62.5±0.05	31.25±0.05
Ph_3Sn[4-NO_2BzH] [II]	31.25±0.01	7.81±0.05
Nystatin	3.90±0.08	1.95±0.05